

Appl. No. : 09/830,703
Filed : April 26, 2001

AMENDMENTS TO THE CLAIMS

1. **(Withdrawn)** An isolated or purified polynucleotide encoding a mutant mouse parkin2 protein, or a homolog thereof, wherein said mutant causes symptoms of Parkinson's disease.

2. **(Canceled)**

3. **(Withdrawn)** The polynucleotide of claim 1, wherein said polynucleotide is selected from the group consisting of: SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, and SEQ ID NO: 20.

4. **(Withdrawn)** A vector, comprising the polynucleotide of claim 1.

5. **(Withdrawn)** A cell, comprising the polynucleotide of claim 1.

6. **(Withdrawn)** The cell of claim 5, wherein the cell is a prokaryotic or a eukaryotic cell.

7. **(Withdrawn)** A parkin mouse protein, comprising any amino acid sequence selected from the group consisting of: SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, and SEQ ID NO: 34.

8. **(Currently amended)** A transgenic mouse or rat comprising a polynucleotide encoding a mutant mouse parkin2 protein, or a homolog ~~thereof~~ of said mutant mouse parkin2 protein, said polynucleotide comprising a mutation, wherein said mutation causes symptoms of Parkinson's disease when said mutation is present in a human polynucleotide homologous to a polynucleotide of SEQ ID NO: 1, and wherein said homolog has an amino acid sequence having at least 70% amino acids identical to said mutant mouse parkin2 protein.

9. **(Canceled)**

10. **(Canceled)**

11. **(Canceled)**

12. **(Canceled)**

Appl. No. : 09/830,703
Filed : April 26, 2001

13. **(Withdrawn)** A mammalian cell-line transformed or transfected with the polynucleotide of claim 1.

14. **(Currently amended)** A method of producing a transgenic mouse or rat, comprising:

constructing a vector that carries an isolated or purified polynucleotide encoding a mutant mouse parkin2 protein, or a homolog ~~thereof~~ of said mutant mouse parkin2 protein, said polynucleotide comprising a mutation, wherein said mutation causes symptoms of Parkinson's disease when said mutation is present in a human polynucleotide homologous to a polynucleotide of SEQ ID NO: 1, and wherein said homolog has an amino acid sequence having at least 70% amino acids identical to said mutant mouse parkin2 protein;

introducing said vector into embryonic stem cells;

injecting said embryonic stem cells into blastocysts;

placing said blastocysts into a pseudopregnant female mouse or rat thereby impregnating said female; ~~and~~

obtaining a pup as a result of such impregnation, wherein said pup is a chimeric mouse or rat, and

mating said chimeric mouse or rat thereby producing the transgenic mouse or rat.

15. **(Previously presented)** A mammalian model for a neurodegenerative disease comprising the transgenic mouse or rat of claim 8.

16. **(Canceled)**

17. **(Withdrawn)** A method for testing the efficacy of a treatment for a neurodegenerative disease, comprising:

subjecting the mammalian model of claim 15 to a putative treatment or agent; and

determining the efficacy of said treatment by identifying a reduction in the symptoms of said neurodegenerative disease.

18. **(Withdrawn)** The method of claim 17, wherein said neurodegenerative disease is selected from the group consisting of: Parkinson's disease, Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis, Multisystem atrophy, Wilson's disease, Pick's disease, and Prion disease.

Appl. No. : 09/830,703
Filed : April 26, 2001

19. **(Canceled)**
20. **(Withdrawn)** A method for testing whether an active substance is useful for treating the symptoms of Parkinson's disease comprising:
 - administering said active substance to the transgenic animal of claim 8; and
 - determining whether said active substance reduces the symptoms of Parkinson's disease.
21. **(Canceled)**
22. **(Previously presented)** A descendant of the transgenic mouse or rat according to claim 8, wherein said descendant is obtained by breeding said transgenic mouse or rat with the same or any other genotype and wherein said descendant of the transgenic mouse or rat comprises a mutant mouse parkin2 protein or a homologue thereof.
23. **(Withdrawn)** The polynucleotide of claim 1, wherein said mutant comprises a point mutation, deletion or fragment.
24. **(Withdrawn)** The polynucleotide of claim 1, wherein said homolog is human.
25. **(Withdrawn)** The cell of claim 5, wherein said eukaryotic cell is a fungal, insect or mammalian cell.
26. **(Withdrawn)** The cell of claim 25, wherein said fungal cell is a yeast cell.
27. **(Withdrawn)** The cell of claim 25, wherein said prokaryotic cell is a bacterial cell.
28. **(Withdrawn)** The polynucleotide of claim 1, wherein said mutants comprise mutations in exon 1 or exon 3.
29. **(Canceled)**
30. **(Withdrawn)** A method of testing agents for efficacy and toxicity in treating a neurodegenerative disease, comprising:
 - administering said agent to the mammalian model of claim 15; and
 - identifying whether said agent reduces the symptoms of said neurodegenerative disease or is toxic to said mammal.
31. **(Withdrawn)** A method for testing whether an active substance is useful for treating the symptoms of Parkinson's disease, comprising:
 - administering said active substance to the cell-line of claim 13; and

Appl. No. : 09/830,703
Filed : April 26, 2001

determining whether said active substance reduces the symptoms of Parkinson's disease.

32. **(Withdrawn)** The method of claim 20, further comprising testing various dosages of said active substance.

33. **(Previously presented)** The transgenic mouse or rat of Claim 8, wherein said mutation is present in at least one of Exons 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 of SEQ ID NO: 1.

34. **(Previously presented)** The method of Claim 14, wherein said mutation is present in at least one of Exons 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 of SEQ ID NO: 1.

35. **(Canceled)**

36. **(Currently amended)** A transgenic mouse or rat, comprising a polynucleotide encoding a mutant mouse parkin2 protein, or a homolog ~~thereof~~ of said mutant mouse parkin2 protein, said protein comprising a mutation, wherein said mutation causes symptoms of Parkinson's disease when said mutation is present in a human amino acid sequence homologous to an amino acid sequence of SEQ ID NO: 4, and wherein said homolog has an amino acid sequence having at least 70% amino acids identical to said mutant mouse parkin2 protein.

37. **(Previously presented)** The transgenic mouse or rat of Claim 33, wherein said mutation in Exon 4 is a frame-shift mutation.

38. **(Previously presented)** The method of Claim 34, wherein said mutation in Exon 4 is a frame-shift mutation.